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<110> Matsumoto, Yoh-Ichi
 Kimura, Tsuyoshi
 Imaizumi, Atsuchi
 Takedo, Tae
 Co, May Sung
 Vasquez, Maximiliano
 TEIJIN LIMITED

<120> HUMANIZED ANTIBODIES THAT RECOGNIZE VEROTOXIN II AND
 CELL LINE PRODUCING SAME

<130> 019026-000110US

<140> 09700851

<141> 2003-11-03

<150> WO 99/59629

<151> 1999-05-19

<150> US 60/086,570

<151> 1998-05-20

<160> 10

<170> PatentIn Ver. 2.1

<210> 1

<211> 414

<212> DNA

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<222> (1)..(414)

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<223> Figure 1(A): Heavy chain variable region of mouse
 antibody VTm1.1 (MuVTm1.1).

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atg aac ttt gtg ctc agc tcg att ttc ctt gcc ctc att tta aaa gga	48
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly	
1 5 10 15	

gtc cag tgt gaa gtg cag ctg gtg gag tcg ggg gga ggc tta gtg aag	96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys	
20 25 30	

cct gga ggg ccc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc	144
Pro Gly Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe	
35 40 45	

agt agt tat ggc atg tct tgg gtt cgc cag act ccg gag aag agg ctg	192
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu	

50	55	60	
gag tgg gtc gca acc att agt act ggt ggt agt tac acc tac tac cca			240
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro			
65	70	75	80
gac agt gtg aag ggt cga ttc acc atc tcc aga gac aat gcc aag aac			288
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn			
	85	90	95
gcc ctg tat ctg caa atg agc agt ctg agg tct gag gac acg gcc ata			336
Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile			
	100	105	110
tat tac tgt gca aga cgg ggg gac gca tgg ggt aac ttg gac tac tgg			384
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp			
	115	120	125
ggt caa gga acc tct gtc acc gtc tcc tca			414
Gly Gln Gly Thr Ser Val Thr Val Ser Ser			
	130	135	

<210> 2

<211> 138

<212> PRT

<213> Mus musculus

<220>

<223> Figure 1(A): Heavy chain variable region of mouse
antibody VTm1.1 (MuVTm1.1).

<400> 2

Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly			
1	5	10	15
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys			
	20	25	30
Pro Gly Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe			
	35	40	45
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu			
	50	55	60
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro			
	65	70	75
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn			
	85	90	95
Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile			
	100	105	110
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp			
	115	120	125

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
 130 135

<210> 3
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 <212> DNA
 <213> Mus musculus

<220>
 <221> CDS
 <222> (1)..(381)

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 <223> Figure 1(B): Light chain variable region of mouse
 VTm1.1 antibody (MuVTm1.1).

<400> 3
 atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca 48
 Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
 1 5 10 15
 gcc tcc aga ggt gat gtt gtg cta act cag tct cca gcc acc ctg tct 96
 Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
 20 25 30
 gtg act cca gga gat agc gtc agt ctt tcc tgc agg gcc agt caa act 144
 Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
 35 40 45
 att agc aac aac cta cac tgg tat caa cac aaa tca cat gag tct cca 192
 Ile Ser Asn Asn Leu His Trp Tyr Gln His Lys Ser His Glu Ser Pro
 50 55 60
 agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg atc ccc tcc 240
 Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser
 65 70 75 80
 agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc agt atc aac 288
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
 85 90 95
 agt gtg gaa act gaa gat ttt gga atg tat ttc tgt caa cag agt tac 336
 Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Tyr
 100 105 110
 agc tgg ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 381
 Ser Trp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 115 120 125

<210> 4
 <211> 127
 <212> PRT
 <213> Mus musculus

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<223> Figure 1(B): Light chain variable region of mouse
VTm1.1 antibody (MuVTm1.1).

<400> 4

Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

Ile Ser Asn Asn Leu His Trp Tyr Gln His Lys Ser His Glu Ser Pro
50 55 60

Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
85 90 95

Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Tyr
100 105 110

Ser Trp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

<210> 5

<211> 414

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (1)..(414)

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<223> Figure 2(A): Heavy chain variable region of
humanized VTm1.1 antibody (HuVTm1.1).

<400> 5

atg aac ttt gtg ctc agc tcg att ttc ctt gcc ctc att tta aaa gga 48
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

gtc cag tgt gaa gtg caa ctg gtg gag tcg ggg gga ggc tta gtg cag 96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

cct gga ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc act ttc 144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

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agt agt tat ggc atg tct tgg gtt cgc cag gct ccg ggt aag ggt ctg 192
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                55                60

gag tgg gtc gca acc att agt act ggt ggt agt tac acc tac tac cca 240
Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro
    65                70                75                80

gac agt gtg aag ggt cga ttc acc atc tcc aga gac aat tcc aag aac 288
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
           85                90                95

acc ctg tat ctg caa atg aac agt ctg agg gct gag gac acg gcc gta 336
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
           100                105                110

tat tac tgt gca aga cgg ggg gac gca tgg ggt aac ttg gac tac tgg 384
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp
           115                120                125

ggg caa gga acc tta gtc acc gtc tcc tca 414
Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                135

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<210> 6

<211> 138

<212> PRT

<213> Mus musculus

<220>

<223> Figure 2(A): Heavy chain variable region of
humanized VTm1.1 antibody (HuVTm1.1).

<400> 6

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Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
    1                5                10                15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
           20                25                30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
           35                40                45

Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                55                60

Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro
    65                70                75                80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
           85                90                95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
           100                105                110

Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp

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115

120

125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135

<210> 7

<211> 381

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (1)..(381)

<220>

<223> igure 2(B): Light chain variable region of
humanized VTm1.1 antibody (HuVTm1.1) .

<400> 7

atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca 48
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

gcc tcc aga ggt gaa att gtg cta act cag tct cca gcc acc ctg tct 96
Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

gtg tct cca gga gaa aga gcc act ctt tcc tgc agg gcc agt caa act 144
Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

att agc aac aac cta cac tgg tat caa caa aaa cca ggt cag gct cca 192
Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
50 55 60

agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg ata ccc gcc 240
Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala
65 70 75 80

agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc act atc agc 288
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

agt ctg gaa tct gaa gat ttt gca gtg tat tac tgt caa cag agt tac 336
Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr
100 105 110

agt tgg ccg ctc acg ttc ggt caa ggg acc aag gtg gag atc aaa 381
Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 8

<211> 127

<212> PRT

<213> Mus musculus

<220>

<223> Figure 2(B): Light chain variable region of
humanized VTm1.1 antibody (HuVTm1.1) .

<400> 8

Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
50 55 60

Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr
100 105 110

Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 9

<211> 123

<212> PRT

<213> Homo sapiens

<220>

<223> heavy chain variable region of the GF4/1.1 antibody

<400> 9

Glu Val Gln Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Ala Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Pro Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Lys Gly Gly Arg Gln Trp Val Val Leu Gly Tyr Phe Phe Asp Ser
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 10

<211> 110

<212> PRT

<213> Homo sapiens

<220>

<223> light chain variable region of the GF4/1.1 antibody

<400> 10

Glu	Ile	Leu	Met	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
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Glu	Arg	Val	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Asn
		20						25				30			
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
		35				40						45			
Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
	50					55				60					
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Gln	Ser
65					70					75					80
Glu	Asp	Phe	Ala	Leu	Tyr	Tyr	Cys	His	Glu	Tyr	Asn	Gly	Trp	Pro	Pro
				85					90					95	
Trp	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr		
			100					105					110		